

REMARKS

Claims 14, and 18-20 are pending in this application. Claims 14 and 20 were rejected under 35 U.S.C. §101. Claims 14, 19 and 20 were variously rejected under 35 U.S.C. §102(b).

By this amendment, claim 14 has been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendment to claim 14 can be found, *inter alia*, throughout the specification, for example, at page 17, lines 23-28.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and canceled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

The issue of the phenotype of the claimed apo-B100 mutant protein was discussed in the Amendment and Response filed March 5, 2004. The present amendment is made to more distinctly claim the subject matter which Applicants regard as the invention, in particular, specific mutations which account for the mutant phenotype, and to better place the application in condition for allowance. Thus, Applicants respectfully submit that the amendment is does not raise new issues and respectfully request entry of this amendment.

Applicants are grateful to the Examiner for the telephone conversations with Applicants' representative regarding prosecution of the application and proposed amendments. Applicants appreciate the Examiner indicating that claim 18 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants believe that the Examiner's concerns have been addressed as described herein.

Rejection under 35 U.S.C. §101

Claims 14 and 20 were rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. Applicants respectfully traverse this rejection.

Although Applicants believe that the previous claims were directed to statutory subject matter, i.e., an apo-B100 protein comprising a mutation in Site B which results in a proteoglycan–receptor+ phenotype, Applicants have taken the Examiner's suggestion and amended the claims to be directed to an isolated apo-B100 protein comprising a proteoglycan–receptor+ phenotype.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §101.

Rejections under 35 U.S.C. §102(b)

Claims 14 and 19 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Law *et al.* (1990, *J. Lipid Research* 31:1109-1120, "Law"). Claims 14 and 20 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Leroy *et al.* (1992, *J. Lipid Research* 33:889-898, "Leroy") and Law. Applicants respectfully traverse this rejection.

For a claim to be anticipated by a reference, the reference must teach each and every element of the claim.

As discussed throughout the specification, the invention is directed to an isolated apo-B100 protein that comprises a mutation in Site B which results in a proteoglycan–receptor+ phenotype, i.e., an apo-B100 protein with reduced binding activity to proteoglycan but with normal

binding activity to the LDL receptor. Herein, the claims have been amended to specifically point out amino acid alterations in site B of the apo-B100 protein that result in the mutant phenotype.

Thus, the claimed invention is directed to an isolated apo-B100 protein comprising a mutation in Site B, wherein Site B is equivalent to amino acids from about 3358 to about 3369 of the human apo-B100 protein and wherein the mutation comprises at least one amino acid substitution or deletion of at least one of Lys₃₃₆₃, Arg₃₃₆₂, or Arg₃₃₆₄. The claimed invention is also directed to an LDL particle comprising an apo-B100 protein with such a mutation in Site B.

Law describes the amino acid sequence of a number of apo-B100 proteins from a variety of animal species. The Examiner points to the teaching in Law that the rabbit apo-B protein contains two different amino acids in the human equivalent positions 3358 and 3359 and that the pig apo-B protein contains amino acid differences from human at positions 3358, 3359, and 3361. Office Action, page 4. Applicants respectfully submit, however, that Law is silent with regard to an apo-B100 mutant protein as claimed and with regard to an apo-B100 mutation in Site B which results in a proteoglycan– receptor+ phenotype. Thus, Law does not teach the claimed invention.

Leroy describes human and rabbit apo-B100 proteins and LDL particles comprising the proteins. However, as with Law, Leroy is silent with regard to an apo-B100 mutant protein as claimed and with regard to an apo-B100 mutant protein with a proteoglycan– receptor+ activity. Thus, Leroy does not teach the claimed invention.

Accordingly, Applicants respectfully submit that neither Law nor Leroy anticipate the claimed invention.

Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b).

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 220002059710.

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Respectfully submitted,

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